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Adequacy of nutrition support during extracorporeal membrane oxygenation

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Abstract

Background. The use of veno-venous extracorporeal membrane oxygenation (vv-ECMO) is increasing in adults with severe respiratory failure. Observational data suggest that there are significant challenges to providing adequate nutritional support for patients on vv-ECMO. We aimed to describe firstly the nutritional support practices in a large single-centre providing vv-ECMO to adults and secondly any association with clinical outcome.

Methods. We conducted a retrospective review of patients receiving vv-ECMO on the Intensive Care Unit (ICU) of a large London teaching hospital. Adult patients admitted to the ICU with severe respiratory failure between December 2010 and December 2015 were included. Daily energy and protein delivery were compared with estimated targets and reasons for feeding interruptions were collected from electronic medical records. Adequate feeding was defined as 80-110% of estimated targets.

Results. We analysed 203 eligible patients. Median duration of ICU stay was 21.0 (IQR, 15.0–33.0) days and vv-ECMO 10.0 (IQR, 7.0–16.0) days. Although median energy (89.8% (IQR, 80.5–96.0%)) and protein (84.7% (IQR, 74.0–96.7%)) delivery was adequate, underfeeding of either energy or protein occurred on nearly third (28.3%) of nutrition support days. A higher admission severity of illness score was associated with inadequate protein delivery (p=0.040). Patients with more severe organ dysfunction on the first day of vv-ECMO received inadequate energy (p=0.026). The most common reasons for interrupted feeding were medical procedures (39.1%) followed by poor gastric motility (22.8%).

Conclusion. Adequate energy and protein delivery during vv-ECMO is possible but underfeeding is still common, especially in those who are more severely ill or who have more severe organ dysfunction. Patients with inadequate energy or protein intake did not differ in ICU and 6-month survival. Prospective studies investigating optimal feeding in this patient cohort are required.

Introduction

Veno-venous extracorporeal membrane oxygenation (vv-ECMO) is a temporary life support system that removes blood from the central venous circulation and returns oxygenated blood to the right atrium (1). The use of vv-ECMO in adults with severe respiratory failure is increasing, particularly since the H1N1 influenza pandemic of 2009 and 2010 (2, 3). The use of vv-ECMO has led to improved survival among patients with H1N1 (1-3), and importantly has been shown to do so without severe disability at six-months when compared with conventional management (4). However, the overal benefit of ECMO on mortality is inconclusive (5).

In general, patients on the Intensive Care Unit (ICU) are commonly underfed, with data reporting around 50-70% of energy and protein targets are received (6-8). Observational studies demonstrate an association between underfeeding and worse outcomes, including mortality (9, 10). However, these results have not been confirmed in prospective randomised controlled trials (RCTs) over the first week of ICU admission (11-13).

Nutrition support is likely of great importance during vv-ECMO given these patients are some of the most severely ill, are more likely to have a prolonged stay on ICU and may have raised nutritional requirements due to increased protein catabolism secondary to inflammation and acute illness (14). However, despite the rapid increase in use of vv-ECMO since 2010, there remains little information regarding optimal nutritional management of these patients. Guidelines on nutritional support in general critical illness recommend early (within 24–48 hrs) feeding using the enteral route as the first line (15-17). However, there are no specific nutritional guidelines during ECMO; the guidelines by Extracorporeal Life Support Organization simply mention that ‘full energy and protein support is essential’ (18).

To our knowledge, only seven studies have been undertaken investigating nutrition support practices in patients receiving ECMO (19-25). Their findings indicate that despite

timely commencement of enteral nutrition, nutrition deficits are common (19, 20, 22, 24, 25). However, there are important limitations in these studies; some do not report energy and protein intakes separately (19, 20), some data include veno-arterial ECMO (20, 22, 24, 25), whilst other studies include non-ECMO days in their data analysis (24, 25).

Gastrointestinal (GI) intolerances (26) are common causes of underfeeding in the general ICU population and this is also found in patients on ECMO with 50-73% of patients requiring ECMO receiving prokinetic medication (20, 23, 25), however whether this is a result of the severity of illness or due to an effect of ECMO itself is not known.

Our aim was to describe nutritional practices in a single-centre providing vv-ECMO to assess the timing and adequacy of energy and protein delivery through gastric, jejunal and parenteral routes, GI complications during vv-ECMO therapy, and the difference in delivery of energy and protein during and after vv-ECMO. Further, we aimed to investigate the association of nutritional support adequacy with clinical outcome.

Methods

A retrospective observational study of patients receiving vv-ECMO was undertaken on our tertiary mixed medical and surgical intensive care unit which provides the ECMO referral service for 43 hospitals in South East England. The need for informed consent was waived and the study approved by our institutional review committee (reference number 2216).

Inclusion and exclusion criteria

Patients admitted to the ICU with severe respiratory failure requiring vv-ECMO between December 2010 and December 2015 were included if they were age ≥18 years at the time of admission and received ≥72 hours and no more than 6 months of vv-ECMO support. Patients were identified from a prospectively held database and patient records were searched from our electronic intensive care patient information system (ICIP, Philips, Netherlands). Patients were excluded if there was no documentation of calculated

nutritional targets or if they were able to eat and drink for the entire duration of ECMO support.

Nutrition support protocol

Patients on vv-ECMO commenced nutrition support according to the same protocol as general ICU patients which advocates commencing gastric feeding within 24–48 hours of admission, following which individualised nutritional targets were calculated by the ICU dietitian within 48-72 hours of admission. Energy targets were calculated using 25-30 kcal/kg/day during vv-ECMO or during periods of no mechanical ventilation (27), and the Modified Penn State equation (28) was used during periods not on vv-ECMO, but still receiving mechanical ventilation. Protein requirements were calculated using a minimum of 1.2 g/kg/day, with increases depending on clinical condition (e.g. continuous renal placement therapy). For patients with body mass index (BMI) ≥25 kg/m^2, ideal body weight (IBW) and adjusted body weight (ABW) were used to calculate protein and energy requirements, respectively.

Gastric residual volumes (GRVs) were assessed every four hours by nursing staff. Clinical guidelines recommended prokinetic therapy be considered after two GRV >300 ml, and then reducing the rate of feeding after three consecutive GRV >300 ml. If high GRV persisted for more than 72 hours, jejunal feeding (unless contraindicated) followed by parenteral nutrition (PN), was considered. Nasojejunal feeding tubes were placed by nursing staff or ICU dietitian at the bedside using an electromagnetic device (Cortrak, Halyard, UK).

Data collection

All data was retrospectively searched from our electronic patient records (IntelliVue Clinical Information Portfolio, ICIP, Release F.01.00, Philips Healthcare, USA). Age, weight, height and BMI were recorded at the time of admission to the ICU. Severity of critical illness was

calculated using APACHE II (Acute Physiology and Chronic Health Evaluation II) and recorded on the day of ICU admission (29) and the degree of organ failure was calculated using SOFA (Sepsis-related Organ Failure Assessment) and was recorded for the first day of both ICU admission and vv-ECMO therapy (30). Other data collected included gender, principal diagnosis and outcomes such as duration of vv-ECMO therapy, ICU stay, and ICU and six-month survival.

The energy and protein delivered daily for each patient was collected for the days they were on vv-ECMO (always on the ICU) as well for the days following decannulation from vv-ECMO (data only recorded whilst on ICU). The first day of vv-ECMO and the day of vv-ECMO cessation were treated as the first and final day on vv-ECMO, respectively. Data were collected until both oral nutrition commenced and artificial feeding was either ceased, intentionally reduced to provide <100% requirements, or when a patient was discharged from ICU at our institution.

Data on nutritional intake included energy and protein from EN, PN, intravenous (IV) glucose and propofol during a one day period (starting 06:00, finishing 05:59). Energy from propofol was included if it was running at a minimum rate of 10 ml/hr for six or more hours a day. 10% IV glucose was included in energy intake recording if the administered volume exceeded 1000 ml/day.

Daily energy and protein delivery were compared with the estimated target that day. If targets were expressed as a range, the midpoint of the range was recorded. For the first day on the ICU, nutritional targets were re-calculated as a proportion of a 24-hour period based on the time of admission, in order to ensure correct data representation. Similarly, on the patient's last day on the ICU, nutritional targets were re-calculated as the proportion of a 24-hour period based on the time of discharge or death.

The overall energy and protein targets for periods on vv-ECMO and post vv-ECMO, were recorded as the mean of each period. The overall energy and protein delivery for these periods was also recorded as the mean of each period.

Adequate delivery of nutrition was defined as 80-110% of the target of energy or protein for that day, with underfeeding defined as <80% and overfeeding >110%. Although the optimal energy and protein intake in critical illness is much debated (31), recent studies have observed lower 60-day mortality when 80% of energy (32) and protein (8) targets were achieved. The upper limit of 110% was chosen to account for inaccuracies in estimated weight based targets. When analysing nutrition support days, patients who were underfed either energy or protein (e.g. underfed energy/ adequate protein and underfed energy/overfed protein) were categorised as underfed.

The time taken to reach adequate energy and protein delivery over a 24-hour period was calculated from the time of admission to the first hour of the 24-hour period of adequate delivery.

The main, second and third routes of feeding during vv-ECMO were recorded based on the length of time a patient relied on any one route. The longest duration of any one route was recorded as the main route. Special attention was paid to capture possible reasons for underfeeding. The number, duration and main reason for feeding interruptions during vv-ECMO were recorded. The main reason was defined as the reasons for the longest interruptions. If EN was stopped or reduced due to GRV >300 ml, three preceding values and name/dose of a prokinetic agent administered, were recorded.

Statistical Analysis

Data were analysed using SPSS, version 23 (IBM SPSS Software NY, USA). Categorical data are presented as *n* (%), continuous data as mean (standard deviation [SD]) for normally distributed data and median (interquartile range [IQR]) for non-normally distributed data. Assumptions for normality were assessed using Kolmogorov-Smirnov One-Sample test.

Categorical data were compared between two groups using Chi-squared test. Continuous data, which was not normally distributed, were compared between two groups

using Mann-Whitney test and between three groups using Kruskal-Wallis test and Bonferroni *post hoc* correction. Nutritional delivery during vv-ECMO and post vv-ECMO were compared using the Wilcoxon Signed Ranked test or sign test (where distribution was asymmetrical on inspection of a histogram). $P < 0.05$ was considered statistically significant.

Results

241 patients received vv-ECMO between December 2010 and December 2015. Of the 241 patient records assessed for eligibility, 38 were excluded (18 <72h on vv-ECMO, seven no estimated nutrition target, five <18 years of age, three received oral nutrition only, two had incomplete nutrition delivery data, one incorrect medical number, one with oral nutrition intake during vv-ECMO and supplementary or no artificial nutrition, and one > six months on vv-ECMO) resulting in 203 patient records included in this analysis.

Two hundred and two patients were admitted for medical reasons and one was admitted for surgery. Details of the demographic and baseline data of all included patients are shown in Table 1.

214 **Table 1.** Demographic and baseline clinical data of 203 patients.

Characteristics	Result
Age (year), median (IQR)	44.0 (33.0–55.0)
Gender, *n* (%)	
Female	91 (44.8)
Male	112 (55.2)
Weight (kg), median (IQR)	80.0 (65.0–100.0)
BMI (kg/m^2), median (IQR)*	27.0 (23.7–33.0)
Principal diagnosis	
Aspiration, *n* (%)	11 (5.4)
Asthma, *n* (%)	14 (6.9)
Influenza, *n* (%)	35 (17.2)
Pneumonia, *n* (%)	94 (45.3)
Sepsis, *n* (%)	12 (5.9)
Other infectious respiratory failure, *n* (%)	10 (4.9)
Other respiratory failure, *n* (%)	29 (14.3)
APACHE II score, median (IQR)	18 (15–21)
SOFA score on admission, median (IQR)	6 (4–11)
SOFA score on first day of vv-ECMO, median (IQR)	7 (4–11)
vv-ECMO duration (days), median (IQR)	10.0 (7.0–16.0)
ICU duration (days), median (IQR)	21.0 (15.0–33.0)
vv-ECMO survival, *n* (%)	172 (84.7)
ICU survival, *n* (%)	163 (80.3)
Six-month survival, *n* (%)	159 (78.3)
Estimated energy requirements (kcal/day), median (IQR)	1800 (1600–2000)
Estimated protein requirements (g/day), median (IQR)	87.0 (75.0–100.0)

**n=202;* BMI for one patient unknown

APACHE II: Acute Physiology and Chronic Health Evaluation II; BMI: Body Mass Index; ICU: Intensive Care Unit; SOFA: Sepsis-related Organ Failure Assessment; vv-ECMO: veno-venous extra corporeal membrane oxygenation.

215

216

Nutrient delivery and adequacy during vv-ECMO

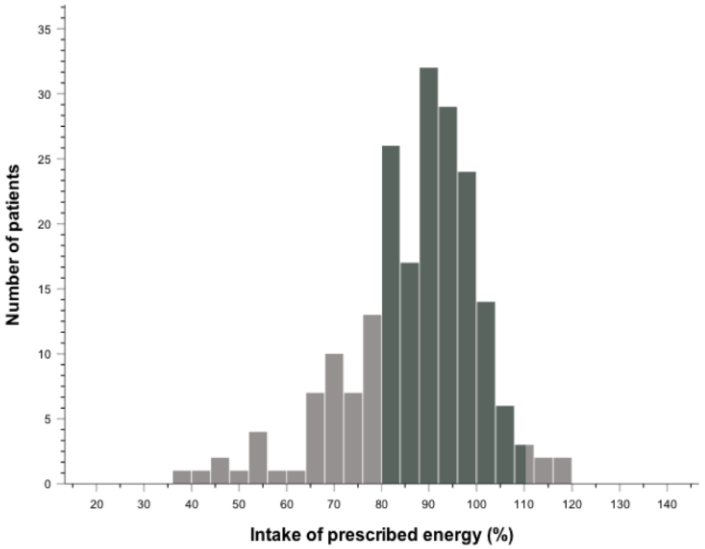
VV-ECMO support was provided on a total of 2989 days, which consisted of 2900 days of artificial nutritional support (EN, PN). During these nutritional support days on vv-ECMO the median energy delivered was 89.8% (IQR 80.5–96.0%) and protein 84.7% (IQR 74.0–96.7%) of targets (Table 2). However, underfeeding still occurred in a large proportion of patients (Figure 1). Protein and/or energy intake was inadequate on approximately one quarter of days (Table 2).

Table 2. Energy and protein intake from nutritional support and adequacy during vv-ECMO of all 203 patients included in the study.

	Outcomes
Energy intake whilst on vv-ECMO	
Overall intake (% of target), median (IQR)	89.8 (80.5–96.0)
Minimum – maximum (% of target)	37.0 -119.3
Energy from IV glucose, median (minimum – maximum) (kcal/patient)	0.0 (0.0 – 3692.4)
Energy from propofol, median (minimum – maximum) (kcal/patient)	0.0 (0.0–2290.9)
Cumulative energy balance whilst on vv-ECMO[a] (kcal), median (IQR)	−1625.6 (−4088.3 to −540.0)
Protein intake whilst on vv-ECMO	
Overall intake (% of target), median (IQR)	84.7 (74.0–96.7)
Minimum – maximum (% of target)	25.9-133.8
Cumulative protein balance whilst on vv-ECMO (g), median (IQR)	−117.1 (−222.9 to −22.1)
Adequacy of energy intake, n (%) days[b]	
Underfeeding	694 (23.9)
Adequate feeding	1830 (63.1)
Overfeeding	376 (13.0)
Adequacy of protein intake, n (%) days[b]	
Underfeeding	790 (27.2)
Adequate feeding	1439 (49.6)
Overfeeding	671 (23.1)
Adequacy of energy and protein intake, n (%) days[b]	
Underfeeding either energy or protein	822 (28.3)
Adequate feeding both energy and protein	1203 (41.5)
Overfeeding either energy or protein	875 (30.2)

[a] Balance calculated as the difference between estimated target and delivery

[b] Total number of nutrition support days was 2900



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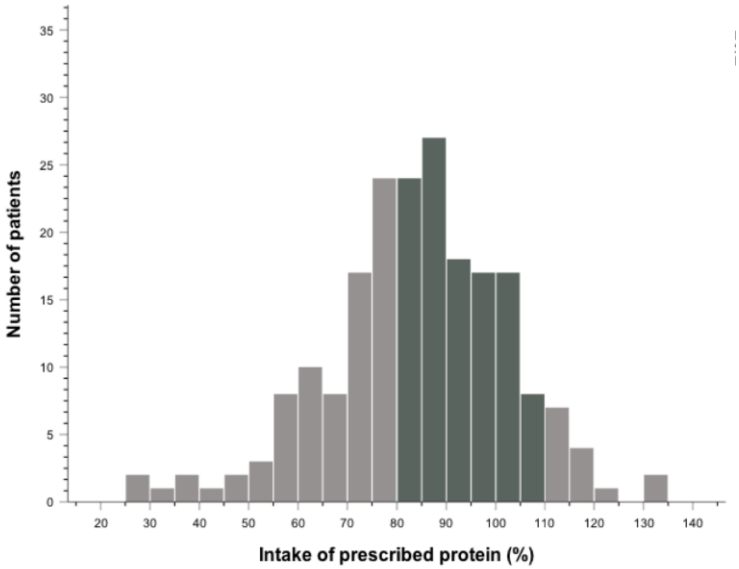

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Figure 1. A: Distribution of mean intakes of prescribed energy (A) and protein (B) per patient during vv-ECMO. Feeding was considered adequate if 80-110% of estimated targets were met (highlighted in dark grey).

The median time taken to start nutritional support was 13.5 hours (IQR, 9.0–23.5) and 197 patients (96.6%) received nutrition support within 48 hours. The median time to reach adequate intake of both energy and protein over a 24-hour period was 68.8 hours (IQR, 41.5–105.8), although 13 (6.4%) patients never achieved adequate intake. The

median time taken to reach adequate energy intake was 54.5 hours (IQR, 36.0–77.8) (five (2.5%) patients excluded due to never achieving adequate intake) and for protein was 59.5 hours (IQR, 36.9–86.0) (11 (5.4%) patients excluded due to never achieving adequate intake).

Route of feeding

The most common route of feeding during vv-ECMO was gastric (123 patients, 60.6%) followed by jejunal (70 patients, 34.5%) and parenteral (10 patients, 4.9%). Jejunal feeding was attempted in another 20 (9.9%) patients but was unsuccessful as the clinician was not able to advance the tube post-pylorically and therefore, the gastric route was used. Two patients were admitted with a long-term EN feeding tube – one percutaneous endoscopic gastrostomy tube and the other percutaneous endoscopic jejunostomy tube.

Nutritional adequacy and outcomes

Patients whose median protein intake represented underfeeding (<80% requirements) (n=78) had higher APACHE II score on ICU admission than those with adequate (n=111) (p=0.040), and patients whose average energy intake represented underfeeding (n=48) had higher SOFA score on the first day of vv-ECMO than those with adequate (n=150) (p=0.026). Patients with inadequate energy or protein intake did not differ in the time taken to start nutritional support or ICU and 6-month survival (Table 3). However, those with adequate energy (p<0.001) and protein (p=0.001) delivery had longer duration of vv-ECMO than those without (Table 3).

264 **Table 3.** Associations between outcomes and adequacy of energy and protein delivery during vv-ECMO.

	Energy[a]		p value	Protein[b]		p value
	Adequate (80–110% of target)	Underfeeding (<80% of target)		Adequate (80–110 % of target)	Underfeeding (< 80 % of target)	
Number of patients, n (%)	150 (73.9)	48 (23.6)		111 (54.7)	78 (38.4)	
Disease severity scores, median (IQR)						
APACHE II score	18.0 (15.0–20.0)	19.0 (15.0–22.8)	0.113[a]	18.0 (14.0–20.0)	19.0 (16.0–22.0)	0.040[c]
SOFA score on admission	5.5 (4.0–11.0)	8.0 (4.0–11.0)	0.117[a]	6.0 (4.0–11.0)	8.0 (4.0–12.0)	0.440[c]
SOFA score on first day of vv-ECMO	7.0 (4.0–11.0)	9.0 (5.0–12.0)	0.026[a]	7.0 (4.0–11.0)	8.5 (4.0–12.0)	0.201[c]
vv-ECMO duration, median (IQR)	11.0 (8.0–18.0)	8.0 (6.0–10.0)	<0.001[a]	11.0 (7.0–17.0)	8.0 (7.0–12.0)	0.001[c]
ICU duration, median (IQR)	23.0 (15.0–36.8)	18.5 (11.3–38.8)	0.052[c]	21.0 (15.0–33.0)	20.5 (14.0–30.3)	0.304[c]
Survival						
Whilst on vv-ECMO, n (%)	124 (82.7)	43 (93.8)	0.129[c]	92 (82.9)	67 (85.9)	0.577[d]
Whilst on ICU, n (%)	119 (79.3)	39 (81.3)	0.773[c]	88 (79.3)	62 (79.5)	0.972[d]
At six-months, n (%)	116 (77.3)	38 (79.2)	0.790[c]	86 (77.5)	61 (78.2)	0.906[d]

[a] Five patients, who were overfed energy (>110% of target), were excluded from analysis due to low numbers

[b] Eleven patients, who were overfed protein (>110% of target), were excluded from analysis due to low numbers

[c] Mann-Whitney test

[d] Chi-squared test

APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: Intensive Care Unit, IQR: interquartile range; SOFA: Sepsis-related Organ Failure Assessment; vv-ECMO: veno-venous extra corporeal oxygenation

265 **Table 3.** Continued.

	Energy		p value	Protein		p value
	Adequate (80–110% of target)	Underfeeding (<80% of target)		Adequate (80–110 % of target)	Underfeeding (< 80 % of target)	
Feeding started from ICU admission (hr), median (IQR)	13.5 (8.9–23.5)	15.5 (10.1–23.1)	0.506[a]	13.5 (8.5–24.0)	15.3 (10.5–23.5)	0.393[a]
Time taken to reach adequate energy and protein intake over a 24-hr period (hr), median (IQR)	69.5 (43.6–105.0) [e]	70.5 (41.3–116.5) [f]	0.492[a]	59.8 (38.1–97.4) [g]	81.5 (50.6–113.0) [h]	0.022[a]

[a] Mann-Whitney test

[e] Nine patients never reached the target. Number of patients 141.

[f] Three patients were never underfed. Number of patients 45.

[g] Seven patients never reached the target. Number of patients 104.

[h] Four patients never underfed. Number of patients 74.

APACHE II: Acute Physiology and Chronic Health Evaluation II; ICU: Intensive Care Unit, IQR: interquartile range; SOFA: Sepsis-related Organ Failure Assessment; vv-ECMO: veno-venous extra corporeal oxygenation

Interruptions to feeding

Feeding interruptions occurred in 184 (90.6%) patients at least once and 95 (46.8%) patients had more than two interruptions. The median number of interruptions during vv-ECMO was two (IQR, 1–4) and the median duration was 9 (IQR, 3.0–32.0) hours. The main reason for interruptions to feeding are shown in Table 4.

Table 4. The frequency of the main reason for interrupting a feed during vv-ECMO.

Main reason for feed interruption	Number of patients (%) (total 184 patients)
Procedures (bedside and operating room)	72 (39.1)
GI intolerances	42 (22.8)
Vomit	19 (10.3)
Concerns over abdominal distention and constipation	12 (6.5)
High gastric residual volume	10 (5.4)
High stool output	1 (0.5)
No access or mechanical complications related to feeding [a]	28 (15.2)
Not documented	16 (8.7)
Investigations	15 (8.2)
GI bleed or blood in aspirate	5 (2.7)
In anticipation of feeding tube extubation	4 (2.2)
Other[b]	2 (1.1)

[a] Mechanical complications such as unable to site feeding tube, feeding tube extubation, tube blockage

[b] Other included hyperglcyaemia and propofol syndrome

Prokinetic agents were used in 106 patients (52.2%). The most commonly used agent was metoclopramide which was used in 104 patients (51.2%). Erythromycin was used in 16 (7.9%) and domperidone was used in one patient (0.4%).

Nutrient adequacy during vv-ECMO vs post vv-ECMO

Overall, 166 patients remained in our ICU post-ECMO. The median energy target for these patients during vv-ECMO was 1800 kcal/d (IQR, 1619–2024kcal/d) and after vv-ECMO decannulation was 1888 kcal/d (IQR, 1650–2100 kcal/d) (p<0.001). The median protein target during vv-ECMO was 88.8 g/day (IQR, 75.0–100.0 g/d), and post-vv-ECMO 88.1 g/day (IQR, 75.0–100.0 g/d) (p=0.253).

There was a small but statistically significant difference in the proportion of energy and protein delivery between the vv-ECMO and post vv-ECMO periods, with median energy delivery during vv-ECMO being 89.8% (IQR, 80.5–96.0%) and post vv-ECMO being 93.4% (IQR, 80.7–101.0%)(p=0.05), and for protein the values were 84.7% (IQR, 74.0–96.7%) and 91.2% (IQR, 74.0–100.6%) (p=0.014), respectively.

Discussion

To our knowledge, this is the largest study investigating the provision of nutrition support in adults receiving vv-ECMO. Our results show that delivery of adequate energy and protein is possible, but underfeeding remains common. Further, we found that a higher APACHE II score on admission to our ICU was associated with lower protein delivery and a higher degree of organ failure on the first day of vv-ECMO with lower energy delivery.

Previous observational studies have reported difficulty achieving nutritional targets in patients receiving ECMO due to frequent feeding interruptions (20, 25). In our cohort, we also report feeding interruptions to be frequent with over 90% of patients having their feed interrupted at least once and almost half having at least two interruptions, for a median duration of 9 hours. Similar to Ridley *et al.* (25) we found fasting for procedures and GI intolerances to be the main reasons for these interruptions. Despite this, we found the median delivery of energy to be 89.8% (IQR, 80.5–96.0%) and protein 84.7% (IQR, 74.0–96.7%) which, according to our *a priori* definition, is considered adequate at the

population level. However, the finding that patients were underfed energy or protein on one in three days during their vv-ECMO highlights that energy and protein debt can still occur, especially following prolonged and repeated feeding interruptions.

It is possible that our higher nutritional intakes compared with others are due to our higher usage of post-pyloric feeding tubes which we have previously reported to be successfully placed at the bedside using an electromagnetic device (33). Results may also have been influenced by changes to our feeding protocol during the period of this study; the protocol was updated to include a high protein enteral formula along with additional dietetic staffing on the ICU allowing 'catch-up' feeding to be prescribed on an individual basis as required.

There was an association between relative underfeeding and reduced length of stay on ECMO. Our results are consistent with an Australian ECMO cohort (24) where increased delivery of energy and protein was associated with longer vv-ECMO support. In addition, we also found the same was true for increased delivery of energy, but not protein and ICU length of stay. The reasons for this are unclear, but one contributing factor may be that the patients who receive vv-ECMO for longer spend a smaller proportion of time achieving a target feeding rate than those who receive vv-ECMO for a shorter time (we did not adjust for duration of vv-ECMO when calculating delivery). Patients may also become more medically stable and require fewer procedures and investigations the longer they receive on vv-ECMO, thus allowing higher nutritional intake.

There was an association between increased severity of illness and adequacy of nutrition, with statistically significantly higher SOFA and APACHE II scores, in the underfed group. Although clearly retrospective observational data is not a demonstration of causality, it is clinically plausible that increased severity of illness results in increased gastric stasis and increased requirement for procedures to be performed.

We found an association between higher APACHE II and SOFA scores and inadequate delivery of protein and energy, respectively. The nutrition risk of these patients should not be discounted. A first glance at the variables contributing to a score such as NUTRIC (age, APACHE II and SOFA) (39, 40) may lead the clinician to classify patients in our cohort as low risk. However, given that the patients in the current study have a prolonged stay both on ECMO and in the ICU, not counting the days in ICU prior to retrieval for ECMO from referring centres, we feel these patients should be classified as high nutrition risk and steps taken to enhance the delivery of nutrition support from ECMO commencement. In addition, nutrition risk only determines mortality, with the effect on muscle wasting and functional outcomes in ICU, on the whole, is currently unknown.

We did not find an association between the adequacy of energy and protein delivery, and either ICU or six-month mortality. This is in contrast to others where an association between improved energy and protein delivery (≥80% of targets) and lower ICU mortality was found for patients on veno-arterial ECMO (27). This may reflect either differences in the severity of illness or the underlying illness (cardiogenic shock compared with acute respiratory distress syndrome) between patients receiving veno-arterial and vv-ECMO.

As previously reported in observational studies of ECMO patients, we found GI intolerances to be a common contributor to feeding interruptions. This was mainly incidence of vomiting and concerns regarding abdominal distention and GI dysmotility which may be a reflection of poor gut perfusion which has been mentioned by others (24).

We found a small, but statistically significant improvement in the delivery of energy and protein in the patients who remained on our ICU post-ECMO, when compared with their stay on ECMO which has been previously reported by others (20). These results may reflect gradual recovery from critical illness and therefore improved GI function and less requirement for procedures, rather than a result of no longer being on vv-ECMO *per se*.

Limitations

The current study has the limitations of being a single-centre, retrospective study. In addition, because nutritional targets for the first day were re-calculated as a proportion of a 24-hour period based on the time of admission, the first day on vv-ECMO was not always representing one whole day. Therefore, the adequacy of feeding expressed as a number of days, may have been overestimated in some cases. Similarly, requirements for both energy and protein are estimated using calculations and usually based on an estimated or previous weight which may influence the results. It is possible that by using a weight-based equation, we have significantly over or underestimated energy targets. Two methods to measure energy expenditure using indirect calorimetry in this population have been described (34, 35), and feeding to measured, rather than calculated, requirements may be one approach to limiting underfeeding or overfeeding in the future. In addition, the protein targets calculated for patients in this study are lower than those recently recommended in the American Society for Parenteral and Enteral Nutrition guidelines. Although the evidence for this recommendation is weak (17), it is entirely plausible that providing higher protein targets for these patients may have resulted in higher protein delivery and improved outcome. Lastly, we have defined adequate energy and protein targets based on currently available evidence for the general critically ill population, but the overall optimal feeding strategy for critically ill patients remains under debate.

Conclusion

Adequate energy and protein intake is possible in patients receiving vv-ECMO support but underfeeding is still common especially in those patients who are more severely ill or have more severe organ dysfunction. As on the ICU in general, not all patients requiring vv-ECMO are the same, underscoring the need for focused research in this area. Studies

investigating the impact of underfeeding on outcomes such as complications and mortality during vv-ECMO could help us to understand the nutritional needs of this patient group.

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Statement of authorship

LK contributed to the design of the research, collection and analysis of the data and drafted the manuscript. DEB contributed to conception/design of the study, collection and interpretation of data and also critically revised the manuscript. KW contributed to the design of the study, supervision of the data collection, analysis and data interpretation, and also critically revised the manuscript. ES, CEH, BS, DO and KD contributed to data collection, interpretation of the data and revision of the manuscript. NAB contributed to the design of the study, interpretation of the results and revision of the manuscript.

Conflict of Interest

DB has received speaker fees from Nutricia, Baxter, BBraun and Fresenius Kabi, conference attendance support from Nutricia, Baxter, BBraun and Fresenius Kabi, consultancy fees from Nutricia, Nestle Nutrition, Abbott Nutrition and Cardinal Health and grant support through her institution from Corpak MedSystems UK. ES has received conference attendance support from Corpak Medsystems UK. NB is a member of the ALung medical advisory board on behalf of his institution; has received research funding through his institution from Corpak, ALung, and Maquet; and has been reimbursed for travel expenses from ALung, Maquet, and Mitsubish Pharmaceuticals. KW has received

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513